



**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

**ATTORNEY DOCKET NO. 072121-0189**

Applicant: Jang HAN et al.

Title: MODIFIED SMALL INTERFERING RNA MOLECULES AND  
METHODS OF USE

Appl. No.: 10/626,879

Filing Date: 07/25/2003

Examiner: Unassigned

Art Unit: Unassigned

**INFORMATION DISCLOSURE STATEMENT**  
**UNDER 37 CFR §1.56**

Commissioner for Patents  
PO Box 1450  
Alexandria, Virginia 22313-1450

Sir:

Submitted herewith on Form PTO/SB/08 is a listing of documents known to Applicants in order to comply with Applicants' duty of disclosure pursuant to 37 CFR §1.56. A copy of each listed document is being submitted to comply with the provisions of 37 CFR §1.97 and §1.98.

The submission of any document herewith, which is not a statutory bar, is not intended as an admission that such document constitutes prior art against the claims of the present application or that such document is considered material to patentability as defined in 37 CFR §1.56(b). Applicants do not waive any rights to take any action which would be appropriate to antedate or otherwise remove as a competent reference any document which is determined to be a *prima facie* art reference against the claims of the present application.

**TIMING OF THE DISCLOSURE**

The listed documents are being submitted in compliance with 37 CFR §1.97(b), before the mailing date of the first Office Action on the merits.

**RELEVANCE OF EACH DOCUMENT**

All of the documents are in English.

Applicants respectfully request that any listed document be considered by the Examiner and be made of record in the present application and that an initialed copy of Form PTO/SB/08 be returned in accordance with MPEP §609.

The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 CFR §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 19-0741. Should no proper payment be enclosed herewith, as by a check being in the wrong amount, unsigned, post-dated, otherwise improper or informal or even entirely missing, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 19-0741.

Respectfully submitted,

November 24, 2003  
Date

FOLEY & LARDNER

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U.S. PATENT DOCUMENTS						
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		Number	Kind Code <sup>2</sup> (if known)			
	A1	5,922,857				
	A2	6,063,628				
	A3	6,506,559				
	A4	2002/0019363				
	A5	2002/0086356				

FOREIGN PATENT DOCUMENTS							
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		Office <sup>3</sup>	Number <sup>4</sup>	Kind Code <sup>5</sup> (if known)			
	A6	WO	01/90121	A2	NOVIRIO PHARMA. LTD.	11/29/2001	
	A7	WO	02/18404	A2	F. HOFFMANN-LA ROCHE AG	03/07/2002	
	A8	WO	02/32920	A2	PHARMASSET LIMITED	04/25/2002	
	A9	WO	02/057287	A2	MERCK & CO., INC.	07/25/2002	
	A10	WO	02/057425	A2	MERCK & CO., INC.	07/25/2002	
	A11	WO	02/100415	A2	F. HOFFMANN-LA ROCHE AG	12/19/2002	

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	A12	AUGERI et al., "Purification, Characterization, Gene Cloning, and Expression of <i>Saccharomyces Cerevisiae</i> Redoxendonuclease, a Homolog of <i>Escherichia Coli</i> Endonuclease III," <i>Biochemistry</i> , Vol. 36, American Chemical Society, 1997, pp. 721-729.		
	A13	BAKER et al., "2'-O-(2-Methoxy) Ethyl-Modified Anti-Intercellular Adhesion Molecule 1 (ICAM-1) Oligonucleotides Selectively Increase The ICAM-1 mRNA Level and Inhibit Formation of the ICAM-1 Translation Initiation Complex in Human Umbilical Vein Endothelial Cells," <i>The Journal of Biochemical Chemistry</i> , Vol. 272, No. 18, May 2, 1997, pp. 11994-12000.		
	A14	BARTENSCHLAGER, et al., "Sequences in the 5' Nontranslated Region of Hepatitis C Virus Required for RNA Replication," <i>Journal of Virology</i> , Vol. 75, No. 24, American Society for Microbiology, December 2001, pp. 12047-12057.		
	A15	BARTON et al., "Retroviral Delivery of Small Interfering RNA Into Primary Cells," <i>Genetics</i> , Vol. 99, No. 23, November 12, 2002, pp. 14943-14945.		
	A16	BHAN et al., "2',5'-Linked Oligo-3'-Deoxyribonucleoside Phosphorothioate Chimeras: Thermal Stability and Antisense Inhibition of Gene Expression," <i>Nucleic Acids Research</i> , Vol. 25, No. 16, Oxford University Press, 1997, pp. 3310-3317		

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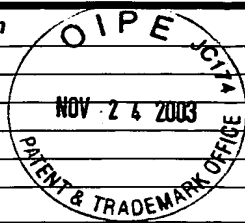
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	A17	CHIANG et al., "Antisense Oligonucleotides Inhibit Intercellular Adhesion Molecule 1 Expression by Two Distinct Mechanisms," The Journal of Biological Chemistry, Vol. 266, No. 27, September 25, 1991, pp. 18162-18171.	
	A18	COLEMAN et al., "Synthesis and Postsynthetic Modification of Oligodeoxynucleotides Containing 4-Thio-2'-Deoxyuridine (d <sup>S4</sup> U)," Journal of American Chemical Society, Vol. 116, 1994, pp. 11636-11642.	
	A19	DAMBA et al., "Properties of Arabinonucleic Acids (ANA & 20'F ANA): Implications for The Design of Antisense Therapeutics That Invoke RNase H Cleavage of RNA," Nucleosides, Nucleotides & Nucleic Acids, Vol. 20, Nos. 4-7, Marcel Dekker, Inc., 2001, pp. 429-440.	
	A20	DECTOR et al., "Rotavirus Gene Silencing by Small Interfering RNAs," EMBO Reports, Vol. 3, No. 12, European Molecular Biology Organization, 2002, pp. 1175-1180.	
	A21	ELBASHIR et al., "RNA Interference is Mediated by 21 and 22-Nucleotide RNAs," Genes & Development, Vol. 15, Cold Spring Harbor Laboratory Press, 2001, pp. 188-200.	
	A22	GIANNARIS et al., "Oligoribonucleotides Containing 2',5'-Phosphodiester Linkages Exhibit Binding Selectivity for 3',5'-RNA Over 3',5'-ssDNA," Nucleic Acids Research, Vol. 21, No. 20, 1993, pp. 4742-4749.	
	A23	GIL et al., "Induction of Apoptosis by The dsRNA-Dependent Protein Kinase (PKR): Mechanism of Action," Apoptosis, Vol. 5, No. 2, Kluwer Academic Publishers, 2000, pp. 107-114.	

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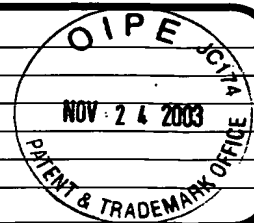
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	A24	KAWASAKI et al., "Uniformly Modified 2'-Deoxy-2'-Fluoro Phosphorothioate Oligonucleotides As Nuclease-Resistant Antisense Compounds With High Affinity and Specificity for RNA Targets," Journal of Medical Chemistry, Vol. 36, American Chemical Society, 1993, pp. 831-841.	
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	A26	Lee et al., "Expression of Small Interfering RNAs Targeted Against HIV-1 rev Transcripts in Human Cells," Technical Report, Vol. 20, No. 5, Nature Biotechnology, May 2002, pp. 500-505.	
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	A28	MIYAGASHI et al., "U6 Promoter-Driven siRNAs With Four Uridine 3' Overhangs Efficiently Suppress Targeted Gene Expression in Mammalian Cells," Nature Biotechnology, Vol. 20, No. 6, May 2002, pp. 497-500.	
	A29	NIKIFOROV et al., "The Synthesis of Oligodeoxynucleotides Containing 4-Thiothymidine Residues," Tetrahedron Letters, Vol. 32, No. 31, Pergamon Press, 1991, pp. 3851-3854.	
	A30	NIKIFOROV et al., "Oligodeoxynucleotides Containing 4-Thiothymidine and 6-Thiodeoxyguanosine As Affinity Labels for The Eco RV Restriction Endonuclease and Modification Methylase," Nucleic Acids Research, Vol. 20, No. 6, Oxford University Press, 1992, pp. 1209-1214.	

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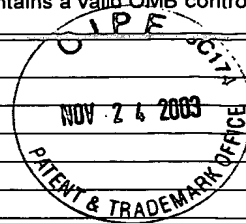
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	A31	PIEKEN et al., "Kinetic Characterization of Ribonuclease-Resistant 2'-Modified Hammerhead Ribozymes," Science, Vol. 253, July 19, 1991, pp. 314-317.	
	A32	SORENSEN et al., "Gene Silencing by Systemic Delivery of Synthetic siRNAs in Adult Mice," J. Mol. Biol., Vol. 327, Elsevier Science Ltd., 2003, pp. 761-766.	
	A33	SVOBODA et al., "Selective Reduction of Dormant Maternal mRNAs in Mouse Oocytes by RNA Interference," Development, Vol. 127, The Company of Biologists Limited, 2000, pp. 4147-4156.	
	A34	TSUCHI, "Expanding Small RNA Interference," Nature Biotechnology, Vol. 30, No. 5, May 2002, pp. 446-448.	
	A35	WANG et al., "Inhibition of <i>Trypanosoma brucei</i> Gene Expression by RNA Interference Using An Integratable Vector With Opposing T7 Promoters," The Journal of Biological Chemistry, Vol. 275, No. 51, December 22, 2000, pp. 40147-40179.	
	A36	WIANNY et al., "Specific Interference With Gene Function by Double-Stranded RNA in Early Mouse Development," Nature Cell Biology, Vol. 2, No. 2, February 2000, pp. 70-75.	
	A37	HOLMES et al., "Coronaviridae: The Viruses and Their Replication," Fundamental Virology, 3 <sup>rd</sup> Edition, Chapter 18, Lippincott-Raven Publishers, 1996, pp. 541-560.	

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